Claims

We claim:

1. A recombinant adeno-associated virus (rAAV)-producing cell,

wherein said rAAV-producing cell comprises a rAAV genome, AAV rep-cap proteins and AAV helper functions,

wherein said rAAV-producing cell expresses AAV Rep 78 and Rep 68 proteins at about the level of expression of the proteins when under the control of the AAV p5 promoter,

and wherein said rAAV-producing cell overexpresses AAV Rep 52 and Rep 40 proteins.

2. A method of producing infectious rAAV comprising the step of culturing a rAAV-producing cell according to claim 1.

3. A method of generating a rAAV-producing cell, comprising the steps of :

a) providing AAV helper functions to a cell comprising a rAAV genome and AAV rep-cap proteins,

b) then subsequently introducing into the cell an expression cassette encoding AAV Rep 52 and Rep 40 proteins.

4. The method of claim 3 wherein the expression cassette in step b) is in a recombinant adenovirus (rAd).

5. The method of claim 4 wherein the rAd is a E3-deleted rAd.

6. The method of claim 5 wherein the E3-deleted rAd of claim X is rAd5/E3/TRE-rep52/40-3.

7. The method of claim 5 wherein the E3-deleted rAd of claim X is rAd5/E3/TRE-rep52/40-5.

8. The method of claim 4 wherein the rAd is a E1-deleted rAd.

9. The method of claim 4 wherein the rAd is derived from simian Ad SV-20 (ATCC VR-199).

10. A method of generating a rAAV-producing cell, comprising the steps of :

a) introducing into a cell comprising a rAAV genome and AAV rep-cap proteins, supplemental AAV Rep 52 and Rep 40 proteins, and

b) providing AAV helper functions to the cell.

11. The method of claim 10 wherein the supplemental AAV Rep 52 and Rep 40 proteins of step a) are introduced by introducing an additional AAV rep52/40 expression cassette into the cell.

12. The method of claim 10 wherein AAV helper functions of step b) are provided by a helper virus of AAV.

13. The method of claim 12 wherein the helper virus of AAV virus is adenovirus (Ad).

14. The method of claim 13 wherein the adenovirus is simian Ad SV-20 (ATCC VR-199).

15. A recombinant E3-deleted Ad stably expressing AAV Rep 52 and Rep 40 proteins.

16. The recombinant Ad of claim 15 that is rAd5/E3/TRE-rep52/40-3.

17. The recombinant Ad of claim 15 that is rAd5/E3/TRE-rep52/40-5.

18. A method of generating a rAAV-producing simian cell comprising the step of:

a) infecting a simian cell stably transformed with a rAAV genome and rAAV rep-cap DNA with a simian Ad.

19. The method of claim 18 wherein the simian Ad is SV-20 (ATCC VR-199).

20. A method of generating a rAAV-producing cell comprising the step of infecting a cell with one or more recombinant adenoviruses and one or more recombinant vaccinia viruses,

wherein the recombinant adenovirus or adenoviruses provide a rAAV genome and AAV cap DNA,

wherein a recombinant vaccinia virus provides rAAV rep 78 DNA, and

wherein either recombinant adenovirus or recombinant vaccinia virus provides rAAV rep 52/40 DNA.

21. A method of producing infectious rAAV comprising the step of culturing a rAAV-producing cell generated by the method of claim 3, 10, 18 or 20.

22. The method of any of claims 2, 3, 10, 20 or 21 wherein said rAAV-producing cells are HeLa cells.

23. The method of any of claims 2, 3, 10, 20 or 21 wherein said rAAV-producing cells are 293 cells.

24. The method of any of claims 2, 3, 10, 20 or 21 wherein said rAAV-producing cells are low passage 293 cells.

25. The method of any of claims 2, 3, 10, 20 or 21 wherein said rAAV-producing cells are PerC.6 cells.

26. The method of any of claims 2, 3, 10, 18, 20 or 21 wherein said rAAV-producing cells are Vero cells.

27. The method of any of claims 2, 3, 10, 18, 20 or 21 wherein said rAAV-producing cells are FRhL-2 cells.

28. The method of any of claims 2, 3, 10, 20 or 21 wherein said rAAV-producing cells are MRC-5 cells.

29. The method of any of claims 2, 3, 10, 20 or 21 wherein said rAAV-producing cells are WI-38 cells.

30. The cell of claim 1 that is a HeLa, 293, low passage 293, PerC.6, Vero, FRhL-2, MRC-5 or WI-38 cell.